



IFw

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Herbert T. Nagasawa and Jonathan F. Cohen
Serial No.: 10/750,005
Filed: December 30, 2003
Docket: 30451.2USU1
Title: METHODS FOR REDUCING OXIDATIVE STRESS IN A CELL WITH A SULFHYDRYL PROTECTED GLUTATHIONE PRODRUG

CERTIFICATE UNDER 37 CFR 1.8

I hereby certify that this paper or fee is being deposited with the United States Postal as first class mail in an envelope addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on July 19, 2004.

By: 
Name: Richelle Ann Domingo

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

We are transmitting herewith the attached:

- ☒ Transmittal sheet, in duplicate, containing Certificate under 37 CFR 1.8.
- ☒ Information Disclosure Statement (37 C.F.R. §1.97 (b)(3))
- ☒ Form 1449 (Information Disclosure Statement) (2 sheets)
- ☒ Exhibits 1 - 19
- ☒ Return postcard

Please charge any additional fees or credit overpayment to Deposit Account No. 50-0306. A duplicate of this sheet is enclosed.

MANDEL & ADRIANO

55 S. Lake Avenue, Suite 710
Pasadena, California 91101
(626)395-7801

By: 

Name: Sarah B. Adriano
Reg. No.: 34,470
Initials: SBA
Customer No.: 26,941



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Herbert T. Nagasawa and Jonathan F. Cohen
Serial No.: 10/750,005
Filed: December 30, 2003
Docket: 30451.2USU1
Title: METHODS FOR REDUCING OXIDATIVE STRESS IN A CELL WITH A SULFHYDRYL PROTECTED GLUTATHIONE PRODRUG

CERTIFICATE UNDER 37 CFR 1.8

I hereby certify that this paper or fee is being deposited with the United States Postal as first class mail in an envelope addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on July 19, 2004.

By: 
Name: Richelle Ann Domingo

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

We are transmitting herewith the attached:

- ☒ Transmittal sheet, in duplicate, containing Certificate under 37 CFR 1.8.
- ☒ Information Disclosure Statement (37 C.F.R. §1.97 (b)(3))
- ☒ Form 1449 (Information Disclosure Statement) (2 sheets)
- ☒ Exhibits 1 - 19
- ☒ Return postcard

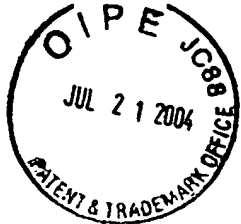
Please charge any additional fees or credit overpayment to Deposit Account No. 50-0306. A duplicate of this sheet is enclosed.

MANDEL & ADRIANO

55 S. Lake Avenue, Suite 710
Pasadena, California 91101
(626)395-7801

By: 

Name: Sarah B. Adriano
Reg. No.: 34,470
Initials: SBA
Customer No.: 26,941

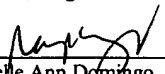


IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Hebert T. Nagasawa et al. **Examiner:** Not yet known
Serial No.: 10/750,005 **Group Art Unit:** 1646
Filed: December 30, 2003 **Docket No.:** 30451.2USU1
Title: METHODS FOR REDUCING OXIDATIVE STRESS IN A CELL WITH A
SULFHYDRYL PROTECTED GLUTATHIONE PRODRUG

CERTIFICATE UNDER 37 CFR §1.8:

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450 on July 19, 2004.


By: Richelle Ann Domingo

INFORMATION DISCLOSURE STATEMENT (37 C.F.R. § 1.97(b)(3))

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Dear Sir:

With regard to the above-identified application, the items of information listed on the enclosed Form 1449 are brought to the attention of the Examiner. They are as follows:

- Anderson, Mary E., "Glutathione and Glutathione Delivery Compounds," *Advances in Pharmacology*, 1997, 38:65-78. – **Exhibit 1**
- Butler, Jean DeBrohun and Stephen P. Spielberg, "Accumulation of Cystine From Glutathione-Cysteine Mixed Disulfide in Cystinotic Fibroblasts; Blockade by an Inhibitor of Gamma-Glutamyl Transeptidase," *Life Sciences*, 1982, 31:2563-70. – **Exhibit 2**
- Chasseaud, L.F., "Reaction with Electrophiles After Enzyme-Catalysed Deacetylation of *N*-acetylcysteine," *Biochemical Pharmacology*, 1974, 23:1133-4. – **Exhibit 3**
- De Rosa, S.C. et al., Abstract of "N-Acetylcysteine Replenishes Glutathione in HIV Infection," *Eur. J. Clin. Invest.*, 2000, 30(10): 915. – **Exhibit 4**

- Eriksson, Stellan A. and Bengt Mannervik, "The Reduction of the L-Cysteine-Glutathione Mixed Disulfide in Rat Liver. Involvement of an Enzyme Catalyzing Thiol-Disulfide Interchange," *FEBS Letters*, March 1970, 7(2):26-8. – **Exhibit 5**
- Eriksson, Bengt and Stellan A. Eriksson, "Synthesis and Characterization of the L-Cysteine-Glutathione Mixed Disulfide," *Acta Chemica Scandinavica*, 1967, 21:1304-11. – **Exhibit 6**
- Fan, Jie et al., "Liposomal Antioxidants Provide Prolonged Protection Against Acute Respiratory Distress Syndrome," *Surgery*, 2000, 128(2):332-338. – **Exhibit 7**
- Herzenberg, Leonore A. et al., "Glutathione Deficiency Is Associated With Impaired Survival In HIV Disease," *Proc. Nat. Acad. Sci.*, 1997, 94:1967-1972 – **Exhibit 8**
- Hudson, Valerie M., "Rethinking Cystic Fibrosis Pathology: The Critical Role Of Abnormal Reduced Glutathione (GSH) Transport Caused By CFTR Mutation," *Free Rad. Biol. Med.*, 2001, 30:1440-1461 – **Exhibit 9**
- Kleinman, Wayne A. and John P. Richie, Jr., "Status Of Glutathione And Other Thiols And Disulfides In Human Plasma," *Biochem. Pharmacol.*, 2000, 60:19-29 – **Exhibit 10**
- Kobayashi, Hiroyuki et al., "The Effects Of Gamma-Glutamylcysteine Ethyl Ester, A Prodrug Of Glutathione, On Ischemia-Reperfusion-Induced Liver Injury In Rats," *Transplantation*, 1992, 54: 414-418 – **Exhibit 11**
- Malorni, Walter et al., "The Role Of Oxidative Imbalance In Progression To AIDS: Effect Of The Thiol Supplier N-Acetylcysteine," *AIDS Res. Human Retroviruses*, 1998, 14:1589-1596 – **Exhibit 12**
- Martensson, Johannes et al., "Glutathione Ester Prevents Buthionine Sulfoximine-Induced Cataracts And Lens Epithelial Cell Damage," *Proc. Nat. Acad. Sci.*, 1989, 86:8727-8731 – **Exhibit 13**
- Nagasawa, Herbert T. et al., "2-Substituted Thiazolidine-4(R)-Carboxylic Acids As Prodrugs Of L-Cysteine. Protection Of Mice Against Acetaminophen Hepatotoxicity," *J. Med. Chem.*, 1984, 27:591-596 – **Exhibit 14**
- Prescott, L.F. et al., "Intravenous N-Acetylcysteine: The Treatment Of Choice For Paracetamol Poisoning," *Br. Med. J.*, 1979, 2:1097-1100 – **Exhibit 15**

- Rathbun, William B. et al., "Maintenance Of Hepatic Glutathione Homeostasis And Prevention Of Acetaminophen-Induced Cataract In Mice By L-Cysteine Prodrugs," *Biochem. Pharmacol.*, 1996, 51:1111-1116 – **Exhibit 16**
- Stein, Aron F. et al., "High-Performance Liquid Chromatographic Analysis Of Glutathione And Its Thiol And Disulfide Degradation Products," *J. Chromatog.*, 1986, 381:259-270 – **Exhibit 17**
- Vina, Jose et al., "Maintenance Of Glutathione Content In Isolated Hepatocytes," *Biochem J.*, 1978, 170:627-630 – **Exhibit 18**
- Williamson, Joanne M. et al., "Intracellular Cysteine Delivery System That Protects Against Toxicity By Promoting Glutathione Synthesis," *Proc. Natl. Acad. Sci. USA*, 1982, 79:6246-6249 – **Exhibit 19**

This statement should be considered because it is submitted before the mailing date of the first Office Action on the merits according to 37 C.F.R. §1.97(b)(3). In accordance with 37 C.F.R. §1.98(a)(2), copies of each document or other information listed on the enclosed Form 1449 are provided.

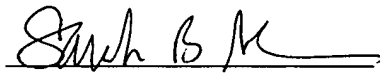
No representation is made that a reference is "prior art" within the meaning of 35 U.S.C. §§ 102 and 103 and Applicants reserve the right, pursuant to 37 C.F.R. § 1.131 or otherwise, to establish that the reference(s) are not "prior art." Moreover, Applicants do not represent that the references have been thoroughly reviewed or that any relevance of any portion of a reference is intended.

Consideration of the items listed is respectfully requested. Pursuant to the provisions of M.P.E.P. § 609, it is requested that the Examiner return a copy of the attached Form 1449, marked as being considered and initialed by the Examiner, to the undersigned with the next official communication.

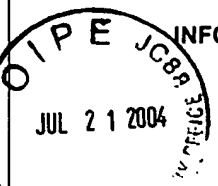
Herbert T. Nagasawa et al.
Serial No. 10/750,005
Filed: December 30, 2003
Page 4

No fee is deemed necessary in connection with the filing of this Information Disclosure Statement. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee, or credit any overpayment, to Deposit Account No. 50-0306.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Sarah B. Adriano", with a long horizontal flourish extending to the right.

Sarah B. Adriano
Registration No. 34,470
Teresa Y. Liang
Registration No. 51,946
Mandel & Adriano
55 S. Lake Avenue, Suite 710
Pasadena, California 91101
(626) 395-7801
Customer No. 26,941

FORM 1449*  INFORMATION DISCLOSURE STATEMENT IN AN APPLICATION (Use several sheets if necessary)	Docket Number 30451.2USU1	Application Number 10/750,005
	Applicant Herbert T. Nagasawa and Jonathan F. Cohen	
	Filing Date December 30, 2003	Group Art Unit 1646

U.S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NO.	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE

FOREIGN PATENT DOCUMENTS

DOCUMENT NO.	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
					YES	NO

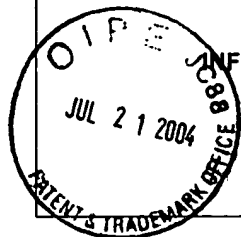
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	Anderson, Mary E., "Glutathione and Glutathione Delivery Compounds," <i>Advances in Pharmacology</i> , 1997, 38:65-78. – Exhibit 1
	Butler, Jean DeBrohun and Stephen P. Spielberg, "Accumulation of Cystine From Glutathione-Cysteine Mixed Disulfide in Cystinotic Fibroblasts; Blockade by an Inhibitor of Gamma-Glutamyl Transeptidase," <i>Life Sciences</i> , 1982, 31:2563-70. – Exhibit 2
	Chasseaud, L.F., "Reaction with Electrophiles After Enzyme-Catalysed Deacetylation of N-acetylcysteine," <i>Biochemical Pharmacology</i> , 1974, 23:1133-4. – Exhibit 3
	De Rosa, S.C. et al., Abstract of "N-Acetylcysteine Replenishes Glutathione in HIV Infection," <i>Eur. J. Clin. Invest.</i> , 2000, 30(10): 915. – Exhibit 4
	Eriksson, Stellan A. and Bengt Mannervik, "The Reduction of the L-Cysteine-Glutathione Mixed Disulfide in Rat Liver. Involvement of an Enzyme Catalyzing Thiol-Disulfide Interchange," <i>FEBS Letters</i> , March 1970, 7(2):26-8. – Exhibit 5
	Eriksson, Bengt and Stellan A. Eriksson, "Synthesis and Characterization of the L-Cysteine-Glutathione Mixed Disulfide," <i>Acta Chemica Scandinavica</i> , 1967, 21:1304-11. – Exhibit 6
	Fan, Jie et al., "Liposomal Antioxidants Provide Prolonged Protection Against Acute Respiratory Distress Syndrome," <i>Surgery</i> , 2000, 128(2):332-338. – Exhibit 7
	Herzenberg, Leonore A. et al., "Glutathione Deficiency Is Associated With Impaired Survival In HIV Disease," <i>Proc. Nat. Acad. Sci.</i> , 1997, 94:1967-1972 – Exhibit 8
	Hudson, Valerie M., "Rethinking Cystic Fibrosis Pathology: The Critical Role Of Abnormal Reduced Glutathione (GSH) Transport Caused By CFTR Mutation," <i>Free Rad. Biol. Med.</i> , 2001, 30:1440-1461– Exhibit 9
	Kleinman, Wayne A. and John P. Richie, Jr., "Status Of Glutathione And Other Thiols And Disulfides In Human Plasma," <i>Biochem. Pharmacol.</i> , 2000, 60:19-29 – Exhibit 10
	Kobayashi, Hiroyuki et al., "The Effects Of Gamma-Glutamylcysteine Ethyl Ester, A Prodrug Of Glutathione, On Ischemia-Reperfusion-Induced Liver Injury In Rats," <i>Transplantation</i> , 1992, 54: 414-418 – Exhibit 11
	Malorni, Walter et al., "The Role Of Oxidative Imbalance In Progression To AIDS: Effect Of The Thiol Supplier N-Acetylcysteine," <i>AIDS Res. Human Retroviruses</i> , 1998, 14:1589-1596 – Exhibit 12
	Martensson, Johannes et al., "Glutathione Ester Prevents Buthionine Sulfoximine-Induced Cataracts And Lens Epithelial Cell Damage," <i>Proc. Nat. Acad. Sci.</i> , 1989, 86:8727-8731 – Exhibit 13

EXAMINER	DATE CONSIDERED
EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form for next communication to the Applicant.	

*Substitute Disclosure Statement Form (PTO-1449) Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

FORM 1449*



INFORMATION DISCLOSURE STATEMENT IN AN APPLICATION

(Use several sheets if necessary)

Docket Number

30451.2USU1

Application Number

10/750,005

Applicant

Herbert T. Nagasawa and Jonathan F. Cohen

Filing Date

December 30, 2003

Group Art Unit

1646

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

Nagasawa, Herbert T. et al., "2-Substituted Thiazolidine-4(R)-Carboxylic Acids As Prodrugs Of L-Cysteine. Protection Of Mice Against Acetaminophen Hepatotoxicity," *J. Med. Chem.*, 1984, 27:591-596 – **Exhibit 14**

Prescott, L.F. et al., "Intravenous N-Acetylcysteine: The Treatment Of Choice For Paracetamol Poisoning," *Br. Med. J.*, 1979, 2:1097-1100 – **Exhibit 15**

Rathbun, William B. et al., "Maintenance Of Hepatic Glutathione Homeostasis And Prevention Of Acetaminophen-Induced Cataract In Mice By L-Cysteine Prodrugs," *Biochem. Pharmacol.*, 1996, 51:1111-1116 – **Exhibit 16**

Stein, Aron F. et al., "High-Performance Liquid Chromatographic Analysis Of Glutathione And Its Thiol And Disulfide Degradation Products," *J. Chromatog.*, 1986, 381:259-270 – **Exhibit 17**

Vina, Jose et al., "Maintenance Of Glutathione Content In Isolated Hepatocytes," *Biochem J.*, 1978, 170:627-630 – **Exhibit 18**

Willamson, Joanne M. et al., "Intracellular Cysteine Delivery System That Protects Against Toxicity By Promoting Glutathione Synthesis," *Proc. Natl. Acad. Sci. USA*, 1982, 79:6246-6249 – **Exhibit 19**

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form for next communication to the Applicant.

*Substitute Disclosure Statement Form (PTO-1449) Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE